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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/902,572	07/10/2001	Avi Ashkenazi	GNE.1618P2C40	5445

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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/902,572	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Daniel M. Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is a reply to the Paper filed 25 April 2006 in response to the Non-Final Office Action mailed 26 October 2005. Claims 39-43 were considered in the 25 April Office Action. Claim 39 was amended in the 25 April Paper. Claims 39-43 are presently pending and under consideration.

Response to Amendment and Arguments

Claim Rejections - 35 USC § 101

Rejection of claim 39 under 35 U.S.C. 101 as directed to non-statutory subject matter is withdrawn in view of the amendment of the claim such that it now recites that the antibody is isolated.

Claim Rejections - 35 USC § 101 and 112, first paragraph

Claims 39-43 **stand rejected** under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for reasons of record and herein below. The *prima facie* rejection was made in the Office Action mailed 26 February 2003.

Response to Arguments

In response to the *prima facie* case and arguments of record, Applicant first contends that the art cited by the Examiner demonstrating the unpredictable nature of establishing protein function based on homology data is irrelevant because Applicant is not relying on homology data

for utility. Thus, it appears that Applicant's position is that the utility for the claimed antibody is based solely on the ability of the polypeptide recognized by the antibody to induce vascular leakage when large quantities are injected into hairless guinea pigs. In the sentence bridging pages 3-4, Applicant states, "Based on positive results obtained in the vascular permeability assay, Applicants had asserted a specific and substantial role for antibodies to PRO302 in stopping vascular leakage in diseases like in pulmonary leakage, capillary leakage, tumor leakage or burns."

These arguments have been fully considered but are not deemed persuasive. As discussed in the previous Office Action (discussion commencing in the paragraph bridging pages 12-13), there is no evidence at all to indicate that the PRO302 polypeptide recognized by the claimed antibody is responsible for vascular leakage associated with pathological states such as tumors or burns such that the utility of anti-PRO302 antagonists to stop vascular leakage or the utility of PRO302 as a target for development of anti-vascular leakage agents is established. The skilled artisan would still have had to confirm that PRO302 plays some role in vascular physiology or pathology as part of its normal functions in the body in order to demonstrate a substantial utility for the protein in identifying antagonists of this particular activity. One cannot consider that developing antagonists to a protein that may only be involved in disrupting vascular integrity upon injection in large quantities under the skin, a completely artificial situation, as a "real world" application in and of itself. For example, it would not be surprising to find that the digestive enzyme trypsin disrupted vascular integrity upon injection in large quantities under the skin in view of its ability to disrupt basement membranes of adherent cells in culture. However, one would not expect that inhibitors of trypsin would have any therapeutic effect in treating

tumors or burns because the enzyme is not present in tumors or burns. Merely demonstrating that a molecule can induce vascular permeability in an artificial system clearly does not substantiate an assertion that antagonists of that molecule are useful in stopping vascular leakage caused by natural processes.

Next, Applicant contends that the Examiner's position is based on an inappropriate standard of proof. Applicant urges that the standards of patentability are not the same as standards of market approval. Applicant cites *Scott v. Finney* and *Nelson v. Bowler* as standing for the propositions that therapeutic utility sufficient under the patent laws is not to be confused with the requirements of the FDA with regard to safety and efficacy of drugs marked in the United States and identification of a pharmacological activity of a compound provides an "immediate benefit to the public" and satisfies the utility requirement.

These arguments have been fully considered but are not deemed persuasive. The arguments rest on the assumption that pharmacological activity has been demonstrated for the claimed antibody. However, as discussed above and in previous Office Actions, the record does not contain any pharmacological data at all for the claimed invention. Furthermore, in *Scott v. Finney*, the issue before the Court was reduction to practice not "substantial utility" and the Court found that the Board erred in suggesting that a showing of reduction to practice requires human testing in actual use circumstances for a period of time. In the instant case, there is no question that no reduction to practice of a therapeutic use for the claimed invention has occurred in any system. Furthermore, the case law cited in *Scott v. Finney* regarding the different roles of the USPTO and the FDA concerns the issue of safety. In contrast, the issue being considered

here is not safety, it is efficacy. Clearly, a determination of whether an invention asserted to be useful as a pharmaceutical could actually be used as a pharmaceutical is relevant to patentability.

Likewise, the facts in *Nelson v. Bowler* are clearly different from the facts in the instant case. In *Nelson v. Bowler*, the CCPA found that the pharmacological activity demonstrated by Nelson was sufficient to satisfy the utility requirement of 35 U.S.C. §101 because, "knowledge of the pharmacological activity of any compound is obviously beneficial to the public". However, in the instant case, no pharmacological activity has been demonstrated. Instead, Applicant merely speculates that, because one can induce vascular permeability by subcutaneous injection of large quantities of PRO302, antagonists of PRO302 might be useful to prevent vascular leakage caused by natural processes. Given no more evidence than what is presently of record, this assertion is no more than the germ of an idea. "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 48 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.')

Finally, Applicant summarizes the Declaration by Sherman Fong, Ph.D., which was submitted with the Paper filed 19 September 2005 and fully addressed in the 26 October Office Action (see the discussion commencing on page 7 and continued through the first full paragraph on page 16).

Applicant's arguments have been fully considered but are not deemed persuasive in view of the record as a whole. Therefore, the claims stand rejected under 35 USC §101 and 112, first paragraph, as lacking a specific and substantial utility.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Friday 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days.

Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Daniel M. Sullivan, Ph.D.
Primary Examiner
Art Unit 1636